REMARKS

Status of the Claims

Claims 1-6 are pending. Claims 2 and 3 are currently amended, and claims 4-6 are added.

Claims 2 and 3 have been amended to better comply with dependent claim format.

New claim 4 depends from claim 3, and recites that the concentration of sodium bicarbonate is 4 mg/ml. Support for this claim is found, for instance, at page 6, lines 15-18 of the Specification

New claim 5 depends from claim 1, and recites the limitation formerly recited in claim 3 that the pharmaceutical composition comprises sodium hydroxide.

New claim 6 depends from claim 5, and recites that the concentration of sodium hydroxide is 1.5 mg/ml. Support for this claim is found, for instance, at page 6, lines 15-18 of the Specification.

No new matter has been added

1. Claim Rejections under 35 USC §112, Second Paragraph

The Examiner has rejected claims 1-3 as allegedly indefinite on the grounds that:

> "...it is unclear what additional ingredients are required, or what other differences there are between a composition is formulated for parenteral administration, and that which is already recited in the claim, i.e., that with the required pH and being free from preservatives and co-solvents." (Office Action, pages 2-3).

Applicants respectfully traverse.

It is well established that, in reviewing claims for compliance with the definiteness requirement of 35 U.S.C. § 112, second paragraph, the Examiner is to focus on whether the claim meets the threshold requirements of clarity and precision. M.P.E.P. § 2173.02 (emphasis added). Further, if the language of the claims can reasonably apprise one of ordinary skill in the art of the scope of the claimed invention, any rejection under 35 U.S.C. § 112, second paragraph is improper. M.P.E.P. §2173.05(b).

With these standards in mind, Applicants point out that the Examiner has imposed the present indefiniteness rejection on the grounds that, when the current form of claim 1 (*i.e.* including the limitation that the pharmaceutical composition it recites is "formulated parenteral administration") is compared to claim 1 in its previous form (*i.e.* not reciting the "formulated for parental administration" limitation), it is unclear what additional ingredients are required or what other differences there are between the current and previous forms of claim 1.

This comparative analysis entirely fails to focus on the clarity and precision of the patentable subject matter actually defined by current claim 1. Instead, it involves a wholly irrelevant analysis of hypothetical differences in the subject matter defined by current and previous forms of claim 1.

The comparative analysis engaged in by the Examiner could perhaps be appropriate in the context of analyzing whether or not a dependent claim further limits the subject matter of a claim from which it depends. But in the context of an indefiniteness rejection of a single claim, a comparative analysis between previous and current forms of claim 1 is irrelevant because it fails to establish that the subject matter actually defined in claim 1 fails to meet threshold requirements of clarity and precision, as required by M.P.E.P. § 2173.02.

Moreover, Applicants submit that current claim 1, directed to a clearly defined pharmaceutical composition formulated for parenteral administration, at least reasonably apprises one of ordinary skill in the art of the scope of the claimed invention, and any rejection of it under 35

U.S.C. §112, second paragraph is therefore improper under M.P.E.P. §2173.05(b). Accordingly, Applicants respectfully request reconsideration and withdrawal of the instant indefiniteness rejection.

2. Claim Rejections under 35 USC §102

2.1 The Anticipation Rejection over Darko (USPN 6,342,530)

The Examiner has maintained his rejection of claim 1 as allegedly anticipated by Darko et al. (USPN 6,342,530). (Office Action, pages 3-4). Applicants respectfully traverse.

As a preliminary matter, Applicants submit that it is impossible for the Darko reference to "make clear" that one particular aqueous solution with a pH range of 6.5 - 8.5 existed, as alleged by the Examiner on page 4 of the Office Action. This is because it is a well-known scientific fact that a given aqueous solution has only one particular pH, which is set by the negative logarithm of the concentration of H^+ ions that solution contains.

Applicants also point out that Darko Table 1 independently reports the single pH value for each of two solutions at two time-points: the "Initial" time point for measuring the pH of each solution was February 24, 1998 and the "3 Month" time point for measuring the pH of each solution was July 20, 1998. The two solutions for which Darko Table 1 reports pH values are each comprised of pooled samples of ibuprofen lysinate solutions according to Example 4. (Darko, Column 6, lines 23-29). The "Initial" pH value for one of the two pooled samples is reported to be 7.5, and the "3 Month" pH value for that sample is reported to be 7.3. (Darko Table 1). The "Initial" pH value for the other of the two pooled samples is reported to be N/A, and the "3 Month" pH value for that sample is reported to be 7.3. (See Darko Table 1).

The Examiner seems to be relying upon the disclosure in Table 1 under the heading of the "Limits". As construed in the context of the "pH" parameter, the range stated therein represents

only a quality control range for purposes of rejecting a sample as unacceptable for further processing. That is, the "limits" refers to the range of pH outside of which further manufacture or sale of a batch would be discontinued because the abnormal pH would be indicative of contamination of, or some other problem with, the sample. Applicants emphasize the fact that Darko Table 1 does not report any solution formulated for parenteral administration and having a pH range of 6.5 to 8.5. As discussed above, Darko Table 1 reports the pH values of two samples of finished solutions at two time point to be pH 7.5, pH 7.3, N/A and pH 7.3,; none of these values are within the presently claimed range of pH 8 to 9.

Turning to the legal standards of anticipation, it is well established that anticipation requires that each and every element of the claim at issue is found in a single prior art reference, either expressly or inherently. Kalman v. Kimberly-Clark Corp., 713 F.2d 760, 771 (Fed. Cir. 1983). Anticipation by inherent disclosure is appropriate only when the reference discloses prior art that must necessarily include the unstated limitation, [or the reference] cannot inherently anticipate the claims. Transclean Corp. v. Bridgewood Servs., Inc., 290 F.3d 1364, 1373 (Fed. Cir. 2002). (Emphasis added). That a feature in the prior art reference "could" operate as claimed does not establish inherency; nor is it sufficient if a material [claim] element or limitation is "merely probably or possibly present" in the prior art. In re Robertson, 169 F.3d 743, 745 (Fed. Cir. 1999) and Trintec Indus., Inc. v. Top-U.S.A. Corp., 295 F.3d 1292, 1295 (Fed. Cir. 2002).

With the foregoing points and standards in mind, Applicants point out that Darko expressly discloses only ibuprofen lysinate solutions having a pH adjusted by raising the pH to a point in the range of pH 7.2 – 7.6, with a target pH of 7.4. (Darko, Column 5, line 59 to Column 6, line 2). In addition, Darko Table 1 expressly discloses such solutions having pH 7.3 or 7.5, which is outside the presently claimed solutions of ketoprofen, ibuprofen, naproxen or tiaprofenic acid that have a pH in the range of 8 to 9. It follows that Darko fails to expressly anticipate the presently claimed pharmaceutical compositions.

Under In re Robertson and Trintec Indus., Inc. v. Top-U.S.A. Corp., it is irrelevant to the present anticipation analysis that the solutions disclosed by Darko "could" have a pH in the range of pH 8 to 9. As mentioned above, Darko teaches ibuprofen lysinate solutions adjusted to pH 7.2 – 7.6. The Examiner should note that, such actual examples of the manufacture of solutions by Darko et al. demonstrate a pH of 6.9 upon initial dissolution of the ibuprofen lysinate, and thus the pH is raised to the desired pH of 7.2 to 7.6. It follows that, prior to and after adjustment, the ibuprofen lysinate solutions taught by Darko had a pH of less than 7.6. Darko does not teach adjusting the pH of its ibuprofen lysinate solutions to a point in the range of pH 8 to 9. It follows that no ibuprofen lysinate solution taught by Darko necessarily (or even likely) has a pH in the range of 8 – 9, as presently claimed. Accordingly, under Transclean Corp. v. Bridgewood Servs., Inc. and Trintec Indus., Inc. v. Top-U.S.A. Corp., the Darko reference does not inherently anticipate the presently claimed solutions of ketoprofen, ibuprofen, naproxen or tiaprofenic acid that have a pH in the range of 8 to 9.

In view of the foregoing analysis, Applicants have established that the Darko reference fails to expressly or inherently teach the presently claimed pharmaceutical composition, and therefore, under Kalman v. Kimberly-Clark Corp., Darko is not an anticipating reference. Applicants therefore respectfully request reconsideration and withdrawal of the instant anticipation rejection.

2.2 The Anticipation Rejection over Anarcardio (2003)

The Examiner has rejected claims 1 and 2 as allegedly anticipated by Anarcardio (2003). (Office Action, page 5). Applicants respectfully traverse.

Applicants inform the Examiner that the priority application EP 02023954, filed October 25, 2002, is in English. The priority application may be found online in the EPO database at http://www.epoline.org/portal/public/!ut/p/kcxml/04_Sj9SPykssy0xPLMnMz0vM0Y_QjzKLN4i

3dAfJgFjGpvqRqCKOcAFfj_zcVKBwpDmQ726kH6LvrR-gX5AbGlFunK4IAEFiq1o!/delta/base64xml/L0lDVE83b0pKN3VhQ1NZS0NsRUtDbEVLQ2xFS0NsRUEhL1lOVUlBQUlJSUlJSUlNTUlJSU1JSUNDSUtHS0dPTUVBRUFLQkpCSk9CRk5GTk9GRExETE9EQSEhLzRCMWljb25RVndHeE9VVG9LNzlZUTdEbUc0UjJIS054anNPY2JnbljazNGSUEhIS83XzBfRzIvODgyMjQzL1JET0NTT1JUT1JERVIvZGVzY2VuZGluZy9SRE9DU09SVEZJRUxEL2RhdGUvb3JnZXBvbGluZXBvcnRhbGZyYW1ld29ya3BvcnRsZXRiYXNlU3RhdGVQb3J0bGV0QmFzZUFjdGlvbi9vcmcuZXBvbGluZS5wb3J0YWwuYXBwbGljYXRpb25zLnJlZ2lzdGVycGx1cy5wb3J0bGV0LlJQQWN0aW9uRGlzcGxheURvY3VtZW50TGlzdC9SRE9DRklMVEVSL0luY29taW5n. Unfortunately, the EPO database does not permit download from image files during working hours on the West coast of the U.S., and therefore, no printed copy of the document is provided herewith.

Given that the October 25, 2002 filing date of the priority document for this application is prior to the August 2003 publication date of the Anarcardio reference, Anarcardio is not prior art against the present application. Applicants respectfully request that the Examiner either review the priority document online and withdraw the instant rejection on that basis, or hold the instant rejection in abeyance until a copy of the document can be downloaded and printed by Applicants' Representative.

3. Claim Rejections under 35 USC §112, First Paragraph - Enablement

The Examiner has rejected claims 1 and 2 as allegedly not enabled. The Examiner's detailed reasoning for imposing this rejection appears on pages 6-10 of the Office Action, and is not reproduced here. Applicants respectfully traverse.

Here, Applicants direct the Examiner's attention to the fact that is well established that an applicant's specification is presumptively enabled for the full scope of the claims. In re Marzocchi, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971) (emphasis added). Moreover, the M.P.E.P. specifically states that the Examiner has the initial burden to establish a reasonable basis to

question the enablement of the claimed invention. M.P.E.P. § 2164.04. This reasonable basis must be established by the Examiner "making specific findings of fact, supported by evidence, and then drawing conclusions based on these findings of fact". . . "specific technical reasons are always required." *Id.* Absent such evidence, the burden does not shift to the Applicants. In re Marzocchi, 169 U.S.P.Q. at 369. (Emphasis added).

Applicants point out that, in imposing the enablement rejection, the Examiner cites large amounts of case law. The Examiner also cites the Gentile et al. reference of record for its teaching that compositions of 2-arylproprionic acids generally have a pH at a point in the range of pH 7.0 – 7.5. The Examiner, however, broadly concludes that the present Specification and examples does not provide a person of ordinary skill in the art with sufficient guidance to make the presently claimed solutions of ketoprofen, ibuprofen, naproxen or tiaprofenic acid that have a pH at a point in the range of pH 8 to 9. (Office Action, page 8).

In arriving at this conclusion the Examiner fails to make any specific finding of facts, supported by evidence and/or technical reasons, for finding that the presently claimed subject matter is not enabled. The Examiner fails to explain why a person of ordinary skill in the pharmaceutical arts, having before him a solution of pH 7.0 to 7.5, is not enabled to adjust the pH to the range of 8 to 9. Accordingly, under M.P.E.P. § 2164.04 and In re Marzocchi, the Examiner has failed to establish a *prima facie* case for lack of enablement. Applicants therefore respectfully request reconsideration and withdrawal of the instant enablement rejection.

4. Conclusion

In view of the foregoing remarks, Applicants respectfully request allowance of all the claims, which define subject matter that meets all statutory patentability requirements.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a three (3) month extension of time for filing a reply in connection with the present application, and the required fee is attached hereto.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D. Reg. No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: October 9, 2007

Respectfully submitted,

By /mjn/
Mark J. Nuell
Registration No.: 36,623
BIRCH, STEWART, KOLASCH & BIRCH, LLP
12770 High Bluff Dr., Suite 260
San Diego, CA 92130
(858) 792-8855
Attorney for Applicant

Attachment: pages from priority application